FACTSHEET

REPORT ON CARCINOGENS (RoC)

Year 2001

National Toxicology Program

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NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
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The Report on Carcinogens (RoC), previously called the *Annual Report on Carcinogens*, is prepared in response to section 301 of the Public Health Service Act, as amended. This law stipulates that the Secretary of the Department of Health and Human Services (DHHS) shall publish a report which contains a list of all substances (i) which either are known to be human carcinogens or may reasonably be anticipated to be human carcinogens; and (ii) to which a significant number of persons residing in the United States are exposed. The Secretary of DHHS has delegated responsibility for preparation of the Report to the National Toxicology Program (NTP). The Report on Carcinogens is prepared by the NTP with the assistance of other Federal health research and regulatory agencies and non-government institutions. The listing of a substance in the RoC is descriptive in nature and represents an initial step in hazard identification, which is generally considered the first phase in the analytical process known as risk assessment. The Report is not intended to constitute a risk assessment; it is a hazard identification document only.

The NTP solicits and encourages the broadest participation from interested individuals or parties in nominating agents, substances, mixtures or exposure circumstances for listing in or delisting from the Report on Carcinogens. Nominations submitted to the NTP should contain a rationale for listing or delisting. Appropriate background information and relevant data (e.g. Journal articles, NTP Technical Reports, IARC listings, exposure surveys, release inventories, etc.) which support a nomination should be provided or referenced when possible. Anyone may nominate a substance to be considered for listing in or delisting from the RoC. Nominations for listing or delisting may be submitted to Dr. C.W. Jameson at the address shown below.

The most recent RoC, the 9th Edition, was published in 2000, and may be obtained by contacting the NIEHS Environmental Health Information Service (see below). The 10th Edition is scheduled for publication in 2002. A list of the nominations under consideration for listing in or delisting from the 10th RoC can be obtained by accessing the NTP Home Page at http://ntp-server.niehs.nih.gov or by contacting Dr. Jameson. Nominations received in 2001 will receive consideration for review in 2002. See contact information listed below.

Nominations for listing or delisting may be submitted by any interested party by contacting Dr. C. W. Jameson, NTP, Report on Carcinogens, 79 Alexander Drive, Building 4401, MD EC-14, P.O. Box 12233, Research Triangle Park, NC 27709 phone: (919) 541-4096, fax: (919) 541-0144, email: jameson@niehs.nih.gov.

To obtain the Report on Carcinogens, 9th Edition, contact the NIEHS Environmental Health Information Service P: 919-541-3841, F: 919-541-0273, e-mail: ehis@nih.gov
To subscribe on-line: http://ehis.niehs.nih.gov

Visit the NTP Home Page at http://ntp-server.niehs.nih.gov

REPORT ON CARCINOGENS
CRITERIA FOR LISTING AGENTS, SUBSTANCES, OR MIXTURES

Known to be Human Carcinogens:

There is sufficient evidence of carcinogenicity from studies in humans which indicates a causal relationship between exposure to the agent, substance or mixture and human cancer.

Reasonably Anticipated to be Human Carcinogens:

There is limited evidence of carcinogenicity from studies in humans which indicates that causal interpretation is credible but that alternative explanations such as chance, bias or confounding factors could not adequately be excluded; or

There is sufficient evidence of carcinogenicity from studies in experimental animals which indicates there is an increased incidence of malignant and/or a combination of malignant and benign tumors: (1) in multiple species, or at multiple tissue sites, or (2) by multiple routes of exposure, or (3) to an unusual degree with regard to incidence, site or type of tumor or age at onset; or

There is less than sufficient evidence of carcinogenicity in humans or laboratory animals, however; the agent, substance or mixture belongs to a well defined, structurally-related class of substances whose members are listed in a previous Report on Carcinogens as either a known to be human carcinogen, or reasonably anticipated to be human carcinogen or there is convincing relevant information that the agent acts through mechanisms indicating it would likely cause cancer in humans.

Conclusions regarding carcinogenicity in humans or experimental animals are based on scientific judgment, with consideration given to all relevant information. Relevant information includes, but is not limited to dose response, route of exposure, chemical structure, metabolism, pharmacokinetics, sensitive sub populations, genetic effects, or other data relating to mechanism of action or factors that may be unique to a given substance. For example, there may be substances for which there is evidence of carcinogenicity in laboratory animals but there are compelling data indicating that the agent acts through mechanisms which do not operate in humans and would therefore not reasonably be anticipated to cause cancer in humans.

REPORT ON CARCINOGENS LISTING/DELISTING PROCEDURES

Nominations for listing or delisting an agent, substance, or mixture in the Report on Carcinogens (RoC) should be submitted to the National Toxicology Program (NTP). Nominations must contain a rationale for listing or delisting as either a "known human carcinogen" or a "reasonably anticipated human carcinogen". Appropriate background information and relevant data (e.g. Journal articles, NTP Technical Reports, IARC listings, exposure surveys, release inventories, etc.) which support a nomination should be provided or referenced when possible.

An agent, substance, or mixture nominated for listing or delisting will be evaluated initially by a National Institute of Environmental Health Sciences (NIEHS/NTP) RoC Review Committee (RG1), composed of scientists from the NIEHS/NTP, to determine if the information provided is sufficient to merit further consideration. If it is determined that the nomination contains insufficient information to warrant consideration by the NTP, it will be returned to the original nominator who will be invited to resubmit the nomination with additional justification, which may include new data, exposure information, etc. A notice, stating the action taken for a nominated substance found to contain insufficient justification for consideration, will be published in the Federal Register, trade journals, and NTP news updates, and included in subsequent editions of the RoC with the reason(s) it was not considered further. This decision will also be forwarded to the NTP Executive Committee and the NTP Board of Scientific Counselors.

If it is determined the nomination warrants formal consideration it will be announced in the Federal Register, trade journals, and NTP publications to solicit public comment. The NTP may initiate an independent search of the literature and have a draft background document prepared for the nomination under consideration. NTP RoC background documents will be prepared according to the following general format:

1.0 Introduction
- 1.1 Chemical Identification
  - synonyms, trade names, CAS #'s, molecular formula, molecular structure, etc.
- 1.2 Physical-Chemical Properties
- 1.3 Identification of Metabolites and Structural Analogs

2.0 Human Exposure
- 2.1 Use
- 2.2 Production
- 2.3 Analysis
- 2.4 Environmental Occurrence
  - environmental release, drinking water and food content, consumer products
- 2.5 Environmental fate
  - environmental fates in air, water, and soil
- 2.6 Environmental exposure
- 2.7 Occupational exposure
- 2.8 Biological indices of exposure
- 2.9 Regulations
  - Occupational Exposure Limits (standards and criteria), "other" standards and criteria

3.0 Human Studies
- 3.1 IARC studies
- 3.2 Case control studies
- 3.3 Cohort studies

4.0 Experimental Carcinogenesis
    4.1 Previously reviewed studies
    4.2 Recent Carcinogenicity Studies

5.0 Genotoxicity

6.0 Other Data Relevant to Evaluation of Carcinogenicity and its Mechanisms

Data used in the preparation of Sections 3 through 6 of the draft document must come from publicly available, peer-reviewed sources.

FORMAL REVIEW STEPS

The following describes the review process for nominations that are considered by the NTP for listing in or delisting from the Report on Carcinogens:

NIEHS/NTP RoC Review Committee (RG1)

The original nomination and all public comments received in response to a nomination will be reviewed by RG1. A reviewer for each nomination will be assigned from the RG1 and will be responsible for reviewing the background document and for leading the RG1's discussion of the nomination. Public comments received in response to announcements of the nomination will be reviewed and issues identified will be addressed by RG1. The nomination then continues through the review process.

Nominations reviewed by RG1 for which sufficient information for applying the criteria for listing or delisting could not be obtained will not proceed further. The subsequent RoC review groups, as well as the NTP Executive Committee, will be informed of this action and will have access to the information why it will not proceed further. The original nominator will be notified of the RG1 action and will be invited to resubmit the nomination with additional justification. All nominated agents, substances, or mixtures reviewed by RG1 but not selected for listing or delisting will be included in the subsequent edition of the RoC with the reason(s) why they were not considered further.

NTP Executive Committee's Interagency Working Group for the RoC (RG2)

The second review of nomination is by the NTP Executive Committee's Interagency Working Group. RG2 is a governmental interagency group that assesses whether relevant information on the nominated agent, substance, or mixture is available and sufficient for listing in or delisting from the RoC. A reviewer for each nomination will be assigned from the RG2 and will be responsible for reviewing the background document and for leading the RG2's discussion of the nomination. Public comments received in response to announcements of nominations will also be addressed by RG2 during the review. Upon completion of its review, RG2 will provide comments and recommendations for any changes and/or additions to the background document and also make its recommendations for listing or delisting in the RoC.

Board of Scientific Counselors RoC Subcommittee (External Peer Review)

External peer review will be performed by a subcommittee of the NTP Board of Scientific Counselors. This subcommittee serves as an independent peer review group that assesses whether the relevant information available is sufficient for listing or delisting in the RoC. The subcommittee will review nominations in an open public meeting. Prior to public review, a notice will be published in the Federal Register, trade journals, and NTP publications, soliciting public comment. The notice will also invite interested groups or individuals to submit written comments and/or to address the subcommittee during the public review meeting. Reviewers for each nomination will be assigned from the subcommittee and will be responsible for reviewing the background document and leading the subcommittee's discussion of the nomination. Upon completion of its review, the subcommittee will provide: comments and recommendations for any changes and/or additions to the background document; and recommendations for listing or delisting the nominated agent, substance, or mixture.

Public Comment

Upon completion of the reviews by RG1, RG2, and the Board subcommittee, those nominated agents, substances, or mixtures, which are recommended for listing in or delisting from the RoC, will be published in the Federal Register, trade journals, and NTP publications and final public comment and input on the recommendations will be solicited.

NTP Executive Committee

The recommendations of RG1, RG2, and Board subcommittee, and all public comments received will be presented to the NTP Executive Committee[1] for review and comment.

NTP Director

The Director, NTP, reviews all recommendations and makes final decisions regarding the proposed listing and/or delisting and submits the RoC to the Office of the Secretary, DHHS. The Director, NTP receives the three independent recommendations for the nominations from RG1, RG2, and the NTP Board RoC Subcommittee, and the consensus opinion of the NTP Executive Committee concerning these recommendations. Based on this input and his evaluation of the relevant information, the Director makes his final recommendation of what nominations should be listed in or delisted from the latest edition of the draft RoC and submits it to the Secretary, HHS.

Secretary, Health and Human Services (HHS)

The final draft of the RoC is submitted by the Director, NTP to the Secretary, HHS for review and final approval. Upon approval of the RoC, the Secretary submits it to the U S Congress as a final document. The submission of the RoC to Congress constitutes publication of the Report and it becomes available to the public at that time. A notice of the publication and availability of the latest edition of the RoC, indicating all newly listed or delisted agents, substances, mixtures or exposure circumstances will be published in the Federal Register, trade journals and NTP newsletter publications.

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[1] Agencies represented on the NTP Executive Committee include: Agency for Toxic Substances and Disease Registry (ATSDR), Consumer Product Safety Commission (CPSC), Environmental Protection Agency (EPA), National Center for Environmental Health of the Centers for Disease Control and Prevention (NCEH/CDC), National Center for Toxicological Research of the Food and Drug Administration (NCTR/FDA), National Institute for Occupational Safety and Health/CDC (NIOSH/CDC), Occupational Safety and Health Administration (OSHA), National Cancer Institute of the National Institutes of Health (NCI/NIH), and National Institute of Environmental Health Sciences/NIH(NIEHS/NIH)